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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/365.241	07/30/1999	THOMAS BRODIN	003300-581	1539

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EXAMINER
PONNALURI, PADMASHRI

ART UNIT	PAPER NUMBER
1639	30

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/365,241	Brodin et al
Examiner	**Art Unit**
Padmashri Ponnaluri	1639

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jan 10, 2003* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *65-94* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *65-94* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

NOTE: The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1639.

1. The preliminary amendment E filed on 7/18/02; and amendment F, filed on 1/10/03 has been fully considered and entered into the application.

2. Claims 1-4, 6-7, 9-10, 17-27, 29, 33-57 and 61-64 have been canceled; and new claims 65-94 have been added by the amendment E filed on 7/18/02.

3. Claims 65-94 are currently being examined in this application.

4. Applicant's election with traverse of species for antibody identifying sequence information of nucleic acid in Paper No. 28, filed in 10/28/02 is acknowledged. The traversal is on the ground(s) that there is not serious burden on the examiner. This is not found persuasive because the requirement made was not under restriction, the requirement was made under species election. The species election between different groups is proper, because the art references which read on one species would not be obvious over the other species. If applicants believe that the species are

not patentably distinct, applicants should submit evidence or identify such evidence now of record showing the species to be obvious variants.

And further applicants argue that the instant claims are drawn to a general method, thus two different species of tag (sequence identifying information) can be used with the general method. Applicants arguments are not persuasive, because the instant claimed method is not yet found allowable, and the species election would be required for search, since the generic method is not searchable. Upon identifying the generic method claim is allowable, all the species encompassed by the genus would be allowed with the generic method.

Applicants arguments regarding the monoclonal antibody has been considered, but are moot in view of the amendments made by applicants.

The requirement is still deemed proper and is therefore made FINAL.

5. This application has been filed with informal drawings. Applicant is invited to notice that boxes 10, 12 were checked by the draftsman in PTO 948. If applicant renumber the figures, applicant is encouraged to amend the specification so that the description of renumbered figure corresponds to the renumbered figures.

6. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

7. The listing of references in the specification is not a proper information disclosure statement. 37 CAR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 65-94 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 65 recites 'scFv/Fab fragment thereof'. It is not clear what does applicants mean by 'fragment thereof', because the scFv or fab are fragments of an antibody. Does applicants mean fragments of ScFv or ScFab. If they are the fragments of either ScFv or ScFab it is not clear which portions of the ScFv or the ScFab are acquired in the claimed invention.

Claim 65 recites 'target structure', applicants are requested to clarify what are the target structures. And the claimed method steps do not recite antibody or fragments of antibody bound to the target structures. Applicants are requested to clarify.

In the claimed method steps recite in step a) exposing a first mounted tissue to an initial antibody library; step F) recites exposing the enriched elements to a second mounted tissue.

However it is not clear whether the 'first mounted tissue and the second mounted tissue' are different from each other. And if they are the same what is the difference between the 'third enriched library' and 'fourth enriched library' from the first and second enriched libraries. If applicants want to use two different mounted tissue applicants are requested to amend the claim. Further it is not clear whether the mounted tissue contains the target or not. Applicants are requested to amend the claim, such that the target is present in the first and second mounted tissue however the first mounted tissue and second mounted tissue are different.

The instant claimed method is vague and indefinite, according to the instant claimed method of acquiring a monoclonal antibody to a target comprises:

a) exposing a first mounted tissue to an antibody library;

b) eluting the unbound elements to the first mounted tissue(first enriched library);

c) recovering the bound elements to the first mounted tissue (second enriched library) and the monoclonal antibody remains bound to the first mounted tissue (interpreted as that an antibody from the library is left uncleaved to the mounted tissue);

d) amplifying first and second enriched libraries;

e) repeating steps A) to B) to negatively enrich or repeating steps A) to C) to positively enrich;

f) exposing the positively and negatively enriched to a second mounted tissue;

g) eluting the unbound elements to the second mounted tissue(third enriched library);

h) recovering the bound elements to the mounted tissue (fourth enriched library) and the monoclonal antibody remains bound to the second mounted tissue (interpreted as that an antibody from the library is left uncleaved to the mounted tissue);

I) isolating an individual element from either the third or fourth enriched libraries, wherein the individual element is the monoclonal antibodies.

The claimed method seem to be having several problems. Initially in step c) recites that the monoclonal antibody remains unbound to the first mounted tissue. Thus the monoclonal antibody to the target is acquired. Does applicants mean that the bound elements comprise the monoclonal antibody to the target and the bound elements are cleaved from the mounted tissue.

Further it is unclear according to the last step I) how a monoclonal antibody to the target is isolated or identified from the third enriched library which contains only unbound elements to both the first mounted tissue and second mounted tissue. Applicants are requested to amend the claim such that the method steps are clear.

Claim 69 recites the limitation "the target structure of the first and second mounted tissue" in line 2. There is insufficient antecedent basis for this limitation in the claim or in claim 65. Claim 64 does not recite how the target structure is related to the mounted tissue. Applicants are requested to clarify.

Claim 69 recites 'binding pattern', applicants are requested to clarify, what does applicants mean by 'binding pattern'. The binding pattern is compared as binding constants or some other structural aspects of binding is characterized.

Claim 91 recites the limitation "the recovered bound element". There is insufficient antecedent basis for this limitation in the claim or in claim 65.

Claim 92 recites the limitation "the coverage occurs" . There is insufficient antecedent basis for this limitation in the claim or in claim 65.

Claim 93 recites the limitation "the cleavage" . There is insufficient antecedent basis for this limitation in the claim or in claim 65.

Claim 95 recites the limitation "the elution" . There is insufficient antecedent basis for this limitation in the claim or in claim 65.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 87-90 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims briefly recite that the initial antibody library further comprises antibody identifying information.

The specification discloses methods for acquiring a monoclonal antibody to a target by screening an antibody library with mounted tissue. However, the specification does not disclose any initial library comprising amino acid sequence or nucleic acid sequence which identifies an

antibody, which would not meet the written description provision of 35 U.S.C 112, first paragraph.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

Adequate written description requires more than a mere statement that it is part of the invention. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008,

1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, the initial antibody library comprising sequence identifying information as claimed in claims 87-90 do not meet the written description provision of 35 U.S.C 112, first paragraph.

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 65-76, 78-80, 84-86, and 91 are rejected under 35 U.S.C. 102(b) as being anticipated by Cai et al (PNAS, Vol. 93, pp 6280-6285, June 1996).

The instant claims briefly recite a method of acquiring a monoclonal antibody to a target comprises:

a) exposing a first mounted tissue to an antibody library;

b) eluting the unbound elements to the first mounted tissue(first enriched library);

c) recovering the bound elements to the first mounted tissue (second enriched library) and the monoclonal antibody remains bound to the first mounted tissue (interpreted as that an antibody from the library is left uncleaved to the mounted tissue);

d) amplifying **either the first or second enriched libraries**;

e) repeating steps A) to B) to negatively enrich **or** repeating steps A) to C) to positively enrich;

f) exposing the positively **or** negatively enriched to a second mounted tissue;

g) eluting the unbound elements to the second mounted tissue(third enriched library);

h) recovering the bound elements to the mounted tissue (fourth enriched library) and the monoclonal antibody remains bound to the second mounted tissue (interpreted as that an antibody from the library is left uncleaved to the mounted tissue);

I) isolating an individual element from either the third **or** fourth enriched libraries, wherein the individual element is the monoclonal antibodies.

Cai et al teach a melanoma specific VH antibody cloned from a fusion phage library of a vaccinated melanoma patient. The reference teaches human antimelanoma antibody V86 cloned form a single chain Fv molecule fusion phage library (refers to initial antibody library of the instant claims) (refers to instant claims 84-85) displaying the heavy chain variable domain and light chain variable domain of a mealnoma patient. The reference teaches that tissue sections cut from the frozen tissue cells of melanoma tumors or normal skin (refers to mounted tissue of the instant

claims 80) and are used for immunohistochemistry which followed the method steps of cultured cells. That is the frozen tissue exposed to the V86 phage library. The unbound phage washed, and the bound phage was identified.

The reference teaches the Panning method of V86 library (refers to instant claims 66-68). The melanoma cell line (refers to instant claim 75-76) was added to the V86 library, and the unbound phage was removed (refers to step b) of the instant claims). The bound phage was eluted from the cells (refers to step c) of the instant claims). The reference teaches that the eluted phage are amplified (refers to the instant claim step d), and claim 86. The reference teaches that for each subsequent panning step, the amplified phage from the previous panning step were used for panning against mealnoma A2058 cells (refers to steps f-I) of the instant claims).

The reference teaches that the relative binding affinities of the fusion phage antibodies to melanoma cells (refers to the instant claim 69). The reference in figure 1, shows that the immunohistochemical staining of mealnoma DM414 cells with V86 library (panel a); and panel b shows the immunohistochemical staining of melanoma A2058 cells with V86 library. The reference teaches that the melanoma specific binding of V86 was further tested by immunohistochemistry with several of the tumor cell lines ans normal cells. The reference teaches that eh V86 can bind specifically to melanoma cells in a metastatic tumor as well as to cultured melanoma cells in metastatic tumor as well as to cultured melanoma cells (refers to instant claims 70-71 of the instant claims). The reference clearly anticipates the claimed invention.

(NOTE since the instant claimed method does not have to use both the unbound elements and bound elements to enrich or expose to the second mounted tissue, the method would read on panning).

14. No claims are allowed.

15. Applicant's arguments with respect to claims 1-4, 6, 7, 9, 10, 17-57 an d61-64 (now canceled) have been considered but are moot in view of the new ground(s) of rejection.

It is noted that amendment D, filed on 11/19/01 adds new claim 65. Applicants are requested to correct the claim numbers. No two claims should have same number. And furhter claim 65 of amendment D is dependent on the canceeld claim 55.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to P. Ponnaluri whose telephone number is (703) 305-3884. The examiner is on ***Increased Flex Schedule*** and can normally be reached on Monday to Friday from 7.00 AM to 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

P. Ponnaluri
Primary Examiner
Technology Center 1600
Art Unit 1639
19 March 2003

PADMASHRI PONNALURI
PRIMARY EXAMINER